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John Dong

GenPhar, Inc., USA

A tetravalent dengue vaccine induced potent and balanced immune responses against four types of dengue virus

The most effective way to prevent dengue infection and limit the growing epidemics globally is through vaccination. However, there is no effective vaccine available despite that the great efforts have been applied to the research during the past 50 years. The major difficulties that hamper the development of DV vaccine is that there are four genetically and serologically related DV known as DV-1 to DV-4 (or DEN1 to DEN4). Infection by a particular type of DV can induce life-long immunity against the same type. However, this type-specific immunity not only fails to protect against, but also enhance the infections by a different type of DV. Therefore an effective dengue vaccine must balanced immune responses, especially neutralizing responses, against all four types of DV.

To overcome these difficulties, we have developed a vectored tetravalent DV vaccine based on a CAdVax platform that is uniquely capable of expressing multiple antigen inserts (up to six) in a single Ad vector. Our strategy is that CAdVax-mediated transfer of DV antigens (prM,E) of all four serotypes into cells to mimic natural infections by DV and induce long-lasting protective immune responses as seen in DV infections but without the causing the actual disease — "a sheep in the clothing of a wolf". In our preliminary studies, we have shown that vaccination with the tetravalent CAdVax-tetraDV vaccine induced potent neutralizing and CTL responses against four types of DV and protected NHPs against viremia. IND-enabling toxicology and biodistribution studies have also demonstrated the vaccine is well-tolerated at a dose that is 100 times higher than anticipated human dose, and showed no sign of any adverse effects. We will report our progress in late stage preclinical development and plans for future clinical trials.

Biography

Dr. John Dong is President and Chief Scientific Officer of GenPhar, Inc. Under John's leadership, GenPhar, Inc. has developed a unique vaccine platform and created a number of multivalent vaccines against lethal viruses. With a novel technology and promising research data, John has established close collaborations with divisions of the United States Department of Defense (DoD) and National Institutes of Health (NIH). John's collaborations include: working with NIH to develop an HIV vaccine that induces both neutralizing and CTL responses; partnering with the US Army Research Institute of Infectious Diseases (USAMRIID) to develop a multivalent Ebola vaccine and Marburg vaccines; and a joint effort with the US Navy Medical Research Center (NMRC) to develop a tetravalent dengue vaccine against all four serotypes of the dengue virus. John has also been leading the effort to develop commercial applications of the platform, including a hepatitis C vaccine, hepatitis B vaccine and vaccines against other infectious diseases.

dongj@genphar.com